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EVALUATION OF INDIAN MEDICINAL PLANTS IN STRETPTOZOTACINE INDUCED DIABETIC MODELS

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Abstract: Globally, diabetes mellitus (DM) is one of the most prevalent diseases. DM is a prolonged disease caused by inherited and or acquired deficiency of pancreatic insulin production, or due to the inefficacy of the insulin. This study has been undertaken to Screening and isolation of extract from natural products to protect and provide a new rapid diabetic suppression therapy and also study Effect of natural products in streptozotocin induced diabetes models in order to identify its anti-ulcer efficacy.

Keywords- Diabetes Mellitus, streptozotocin, insulin, Anti-diabetic activity, anti-ulcer

INTRODUCTION

DM is characterized by multiple defects in its pathophysiology and abnormalities in carbohydrates, lipids proteins, and metabolism [1–4]. It is evident that this disease leads to hyperglycaemia and to many other complications such as atherosclerosis, hypertension, hyperlipidaemia, neuropathy, retinopathy, and nephropathy. DM depends on several factors such as alterations of people lifestyle, behaviour and environment [3]. Diabetes is a syndrome characterized by disordered metabolism of carbohydrate, protein and lipid with abnormally high blood sugar resulting from low levels of the hormone insulin with or without abnormal resistance to insulin's effect . Diabetes mellitus is considered as one of the five leading causes of death in the world. About 150 million people are suffering from diabetes worldwide, which is almost five times more than the estimates ten years ago and this may double by the year 2030. India leads the way with its largest number of diabetic subjects in any given country. The prevalence of diabetes mellitus is expected to rise more rapidly in the future because of increasing obesity and reduced activity levels [2]

Globally, the World Health Organization (WHO) reports that the prevalence of DM will be increased and by the year 2025 more 300 million individuals will have DM [4]. Medicinal plants have many properties such as the effectiveness, low cost for many diseases and safety.

Remedies from natural products may be effective and safe alternative treatment for DM. Potential impact of such strategies must be first examined in suitable animal models. Several drugs are used to control DM; however, perfect glucose control is rarely achieved [5].

As a result, more and more drugs are coming up offering newer and better options for the treatment of DM, but their critical clinical evaluation has recorded several discrepancies including adverse side effects, and drug interactions. Drugs from native sources of natural products are thus now a target for development, refinement and pharmacological modification for anti-diabetic treatment. The need of new chemical entities (NCEs) for health care is investigated and served through the plant sources. 80% of the populations abiding in the developing countries rely on traditional medicine for their primary health care needs clarified by the World Health Organization (WHO). Roughly estimated that 50% of the NCEs comes during the last two decades are from plant products. In almost all the traditional systems of medicine, the medicinal plants play a major role and constitute their backbone. Indian medicinal plants possess enormous healing power and only a part of this potential is known to mankind. Evolution of Ayurveda and plant-based remedies for health care through day-to-day life experiences is a part of the cultural heritage of India. Various Indian medicinal plants have been reported to possess anti-diabetic activity. Recently, encouragement for using medicinal plants as alternative remedies attributed to the elevation of medication cost, synthetic medicine side influences and lack of full recovery of diabetic patients treated with chemical hypoglycaemic agents [5]. Recently, traditional therapies originated from medicinal showed avital role in the control of DM. Many experimental investigations showed that plants and their leaves, leaves, and their different compounds possessed a large area of pharmacological and therapeutic properties [6].

Traditional medicines most often applies to plants are being employed as adjuvants in the management of diabetes mellitus in many of the Asian countries including India. India has a rich history of using various potent herbs and herbal components for treating diabetes. Medicinal plant or herb have a variety of metabolites, aliphatic compound and aromatic compound, have basic skeleton of organic molecule and have various functional group that makes ability to alter the various metabolic pathway makes them medicinally important. Herbal drugs are prescribed widely because of their effectiveness, less side effects and relatively low cost. Therefore, investigation on such agents from traditional medicinal plants has become more important. In this study we will evaluate the role of natural products in diabetic mellitus.

1.1 History of diabetes:

Diabetes was described in a Egyptian manuscript from c. 1500 BCE focusing on "too great emptying of the urine."[7] The term "diabetes" or "to pass through" was first used in 230 BCE by the Greek Apollonius of Memphis.[7] The disease was considered rare during the time of the Roman empire, This is possibly due to the diet and lifestyle of the ancients, or because the clinical symptoms were observed during the advanced stage of the disease. Galen named the disease "diarrhea of the urine" (diarrhea urinosa).[8] The earliest surviving work with a detailed reference to diabetes is that of Aretaeus of Cappadocia (2nd or early 3rd century CE). He described the symptoms and the course of the disease, which he attributed to the moisture and coldness, reflecting the beliefs of the "Pneumatic School". He hypothesized a correlation between diabetes and other diseases, and he discussed differential diagnosis from the snakebite, which also provokes excessive thirst. His work remained unknown in the West until 1552, when the first Latin edition was published in Venice.[9]

2 MATERIAL AND METHOD

2.1Materials:

2.1.1 Chemicals: Chemicals used in the present study have been listed below along with the name of the manufacturers:

Chemical	Manufacturer
Boric acid	SD Fine Chemicals Ltd., India
Bovine serum albumin	Sigma Chemicals, USA
Bradford's reagent	Sigma Chemicals, USA
Bromophenol blue	Sigma Chemicals, USA

Copper sulphate	Sisco Research Laboratories, India
Dimethyl sulphoxide (DMSO)	Qualigens, India
Ethanol	Merck, Germany
Folin's Reagent	Sisco Research Laboratories, India
Formaldehyde	Sisco Research Laboratories, India
Formamide	Sisco Research Laboratories, India
Glacial Acetic acid	SD Fine Chemicals Ltd., India
Glucose	Sigma Chemicals, USA
Hydrogen peroxide	M.P. Biomedicals, India
Indomethacin	Fluka, USA
Magnesium chloride ($MgCl_2$)	Sisco Research Laboratories, India
Methanol	Merck, Germany
Perchloric acid	Sigma Chemicals, USA
Phenophthalein	Sisco Research Laboratories, India
Potassium dihydrogen phosphate	Sisco Research Laboratories, India
Sodium acetate	Sisco Research Laboratories, India
Sodium Chloride (NaCl)	Sisco Research Laboratories, India
Sodium hydroxide (NaOH)	Sisco Research Laboratories, India
Streptozotocin (STZ)	Sisco Research Laboratories, India
Triton X-100	Sisco Research Laboratories, India

2.1.2 Instruments used in the study:

- Autoclave, Vertical SMI-102 (Jindal, SM Scientific Pvt. Ltd, Delhi, India).
- Digital pH meter (Model- CL-54, Toshniwal Instruments Manufacturing Pvt. Ltd. Chennai, India).
- Electrophoresis chambers (Miniphor UVT System, Maxiphor UVT System Banglore Genei, Banglore, India.
- Freezers (-20ºC Refrigerated, RQFV-265(D), Remi Instruments (-85ºC Ultrafreezer, Model-U41085, New Brunswick, Canada), 4ºC Refrigerators, Samsung India Electronics Pvt. Ltd., New Delhi, India).
- Fluorescent Spectrophotometer (Cary Eclipse Fluorescent Spectrophotometer, PCB 150 Water Peltier System, Varian Inc., the Netherlands).
- Homogenizer with 1/8 Hp motor and auto-transference.
- Ice machine (Ice Boy, Model-ZX-120 ELW, New Delhi, India).
- Incubator (Jindal, SM Scientific Pvt Ltd, Delhi, India).
- Magnetic Stirrer (Remi laboratory Instruments, Mumbai, India).

- Microplate reader (Powerwave ^{TM}-XSL, Biotek India, Mumbai, India).
- Microscopes (Trinocular Stereozoom Microscope SZ-CTV Olympus Optical Co., Tokoyo, Japan).
- Microwave oven (LG Electronics India Pvt. Ltd. Greater Noida, India).
- Spectrophotometer (Shimadzu UV1201, Shimadzu Scientific Instruments, Columbia, USA).
- Shaking Water Bath (LabTech, Diahan Labtech Co. India Pvt. Ltd. New Delhi, India).
- Vortex Mixer (Lead Instrument Pvt. Ltd., Banglore, India).
- Weighing Balances (Micro Electronic Balance, JS 110, Chyo, Japan).

2.1.3 Plants material:

All the plants were collected and the voucher specimen numbers were assigned and preserved in the Herbarium of the Institute. All the extraction procedures of plant extracts were performed. In the present study, the active constituents of plant were used to evaluate their anti-diabetic potential.

2.1.4 Murrya exotica:

The ***Murrya exotica*** were purchased from the local herbal market and the authentification was done by the Institute. The dried leaves of *M. exotica* (1 kg) were keep into small pieces and were placed in glass percolator with 5 lit of ethanol: distilled water (1:1) and allowed to stand at room temperature for 24h. The percolate was collected and this process was repeated for four times. The combined percolate was concentrated under vacuum using rotary evaporator at 40^0C. The weight of extract obtained was found to be 310 gm.

2.2 Methods:

2.2.1 Experimental Animals:

Experimental protocols were approved by the Institutional Ethical and Usage Committee following the guidelines of CPCSEA (Committee for the Purpose of Control and Supervision of Experiments on Animals) which complies with International norms of INSA (Indian National Science Academy). Adult male Sprague Dawley rats, weighing 140–220 g were used in this study. Animals were housed in raised bottom mesh cages to prevent coprophagy and were kept in environmentally controlled rooms with temperature regulated at 22 ± 2◦C, 12/12 h light and dark cycle.

2.2.2 Treatment schedule:

Pilot investigation with the graded doses of test compounds were tested against STZ model to identify the effective dose and selected for further studies. Various test compounds; reference drug Metformin (MET) (10 mg/kg) were freshly prepared in 1% carboxymethyl cellulose (CMC) as suspension and administered orally to the animals. The rats were randomly divided into various groups, each consisting of 6 animals.

2.2.2.1 Treatment groups for diabetic model:

Rats were divided into three groups.

Group I (Control group): Control group of animals were treated with 1% CMC, *for 21 d* after induction of diabetes in rats.

Group II (Treatment groups): Rats were treated with herbal extract M. exotica,. *Rats* administered with STZ (45 mg/kg body weight) intraperitonally. Oral administration of M. Exoctica leaf extract (200 mg/kg body weight) in STZ induced rats from Day 8 to Day 21.

Group III (Reference drug treated): Rats were treated with marketed at metformin (100mg/kg) after 72 hr of streptozotocin treatment.

2.2.2.2 Streptozotocin induced diabetes models:

Male Sprague Dauwley strain albino rats of average body weight 140 ± 20 g having blood glucose profiles between 60 80 mg/dl were selecte. Streptozotocin (Sigma, USA) was dissolved in 100 mM citrate buffer (pH 4.5) and calculated amount of freshly prepared solution of streptozotocin was injected intraperitoneally (i.p.) to overnight fasted rats at a single dose of 45 mg/kg body weight. The animals were allowed to drink 5% glucose solution to overcome the drug induced hypoglycemia. After 72 h of STZ administration, blood samples were collected from tail and glucose levels were estimated by glucostrips (One Touch Glucometer, Life Scan, Europe). Animals having fasting blood glucose levels above 200 mg/dl were considered diabetic and subsequently used in the present study.

2.2.3 Body Weight Measurement:

For body weight evaluation, all experimental animals were weighted at the initiation of the experimental duration and after five weeks. The body weights were recorded at recording time in the morning according to Al-Attar et al [10]. Furthermore, for any signs of abnormalities throughout the duration of investigation, the rats were continuously observed.

2.2.4 Biochemical estimation in streptozotocin induced diabetic models:

Preparation of serum, plasma and tissue homogenate After the experimental period, animals were scarified by cervical decapitation. Blood was collected and centrifuged for serum separation. For plasma, blood was collected with anticoagulant and centrifuged at 2 000 r/min for 20 min. The resulting supernatant was used for the estimation of blood glucose [11,12], cholesterol[13], high density lipoprotein (HDL) and triglyceride[14-15].

Blood glucose profile was checked after 72 hours by glucostrips (Boehringer Mannheim) and animals showing blood glucose values between 150 to 450 mg/dl were included in the experiments and termed diabetic. Blood glucose profile of animals of all groups was again checked at 142 h post administration of test sample. Animals not found diabetic after 48 hours post treatment of the test sample were not considered and omitted from the calculations and termed as non-responders. Food but not water was withheld from the cages during the experimentation.

2.2.5 Antioxidant assays:

Scavenging/Inhibitory activity coefficient: The scavenging or percentage inhibitory activity of in each assay was calculated from:

% Inhibition = (A0 - A1) × 100 / A0

Where A0 = absorbance of the control (without test compounds), and A1 = absorbance of the treated (with test compounds). The IC_{50} value was extrapolated from the standard linear regression curve.

2.2.6 Free radical scavenging activity:

2.2.6.1 DPPH method: The antioxidant activity of the compounds isolated from natural products was assessed on the basis of the radical scavenging effect of the stable DPPH free radical (Blois, 1958). Test compounds or reference (10-100 µg/ml) was added to 200 µl of DPPH in methanol solution (100 M) in a 96-well microtitre plate (Tarsons Product (P) Ltd., India). After incubation at 37°C for 30 min, the absorbance of each solution was determined at 490 nm using ELISA micro plate reader (Bio Rad Laboratories Inc., Model 550, California, USA). The corresponding blank readings were also taken and the remaining DPPH was calculated IC_{50} value is the concentration of the sample required to scavenge 50% DPPH free radical.

Superoxide anion (SOD) scavenging activity assay: Superoxide dismutase activity was measured based on its ability to inhibit the autoxidation of epinephrine to adrenochrome at alkaline pH (Misra and Frdovich, 1972). The absorbance of reaction mixture was followed for 4 min at 480 nm in a spectrophotometer (Model 1201, Shimadzu). Enzymatic activity was expressed as U/mg protein at 30°C. The amount of enzyme that caused 50 percent inhibition of epinephrine autoxidation was defined as one unit (U).

2.2.6.2 Histo-pathological studies

Both control and experimental rats were killed by decapitation and liver tissues were isolated. Liver tissue were dipped into 4% formalin for 24 hr. to stain the liver tissue cut into thin section and kept it on micro tech slides and fixed. Liver tissues were leave for 24h and observed under microscope (10X).

2.2.7 Protein assay:

The Protein content of the samples was estimated by the method of Lowry et al. (1951) using Folin Phenol reagent. Bovine serum albumin (1 mg/ml) was used as standard.

2.2.7.1 Protein estimation of lowery method

This method is reasonably sensitive, detecting 10µg/cm^{-3} of protein. This method is based on the reaction when the folin's reagent together with copper sulphate solution is mixed with protein solution, blue purple colour is formed which can be quantified at 660nm range.

Requirements

BSA Solution (Standard Protein solution), 1mg/ml. Solution A: Mix solution (i) and (ii) 2% Sodium carbonate 0.1N NaOH Solution B: Mix solution (i) and (ii) 1.56% $CuSO_4$ 2.37% Sodium Potassium Tartarate**,** Solution C: Mix 2 ml solution B in 100 ml solution A. **,** Solution D: Dilute Folin Ciocalteau reagent (1:1), at the time of use.

Procedure

Prepare standard solution of stach in increasing concentration and add distilled water to make up volume 1ml in each tube, as shown in table Took 2 ml of solution C in each test tube and added 200 µl of protein solution of each concentration. Incubated for 10 minutes at RT. After incubation added 200 µl of 1X Folin reagent, further incubated for 30 minutes dark. Took the O.D at 660 nm.

2.2.8 Statistical analysis:

Data were expressed as mean ± S.E.M. Analysis will be performed with Prism version 5.0 software using one-way analysis of variance (ANOVA) followed by Dunnett's multiple comparison tests. $P<0.05$ was considered to be statistically significant.

3. RESULTS AND DISCUSSION

3.1 Murrya exotica:

Murraya is a genus of flowering plants, closely related to citrus. *Murraya exotica* are traditionally used in China and its common name is Chinese box. *Murraya exotica* commonly known as Orange Jessamine, is an evergreen, tropical plant with tiny, white, scented flowers, which is cultivated as an ornamental tree. It belongs to the family *Rutaceae* and can be commonly found in Southeast Asia, Northern Asia and Australia. Various parts of this plant have been used in traditional medicine. In Bangladesh *M. exotica* leaves extract is orally used to relieve pain (4). In the Philippines, leaves were also used to treat diarrhoea and dysentery because of their stimulant and astringent activities (4). In India, people sometimes used root bark of *M. exotica* as remedy for coughs, hysteria.

Figure 1: Representative photographs of streptozotocin induced diabetic models

Evaluation of anti-diabetic effect of Murrya exotica against streptozotocin induced diabetic rat model:

Extract of *Murrya exotica* (ME) at graded doses (100, 200 and 400 mg/kg, p.o.) were used and 200 mg/kg showed maximum reduction of glucose level in comparison of others dose. Whereas the metformin (reference drug) reduced the upraised glucose level due to the streptozotocin at 45 mg/kg, i.p. From this observation 200mg/kg dose of ME was identified as the effective dose and selected for further studies.

Whereas Table 1 depicts the treatment schedule and its effect on STZ induced diabetic rats. This study was divided into four group in first group control, it was treated with 1% CMC only and not treated with STZ so the glucose level were normal for the last 21 days. Whereas, glucose level were high in 2nd group STZ only for last 21st days. Furthermore in ME treated group glucose level were not as much high as in STZ only group, it means the ME had potential to reduce the upraise level of glucose. In addition the reference drug metformin significantly reduced the glucose level after treatment of STZ.

Table 1: Effect of ***Murraya exotica*** (ME) extratct and reference drug **Metformin** (Met) on control group after induction of y diabetes. glucose level was monitored after 24 hr, 3rd day, 10th day and 21st day of STZ treatment. (n= 6 in each group).*Statistically significant at P<0.05 and **P< 0.01, in comparison to control. n = 6 in each group.

Treatment	**Glucose mg/dl**			
		Treatment start after 3rd day of STZ		
	24 hr	**3 day**	**10 day**	**21 day**
Control 1% CMC	90.3±08.32	92.7±6.02	89.00±06.23	95.41±09.76
STZ (45 MG/KG)	257.87±06.4	219±28.43	241.0±22.47	238.5±33.21
ME (200 mg/kg)	189.5±30.89*	101.8±66.48	97.50±21.35*	100.20±8.22*
Metformin (100 mg/kg)	88.7±19.28	96.1±37.11	78.30±13.20*	72.50±9.918*

The histological studies were carried out to prove the efficacy of ME leaves extract. Figure 1. Is the photographs of histopathology of liver cells. In image A it depicts a normal liver cell structure. Whereas Image B is STZ-induced diabetic rat and we observed sinusoidal dilation, congestion of portal vessel and hemorrhagic of the liver cells. Further in Image C we found resorted liver cells after the treatment.

Figure 1: Histopathological photographs of rat Livers of streptozotocin induced diabetic models

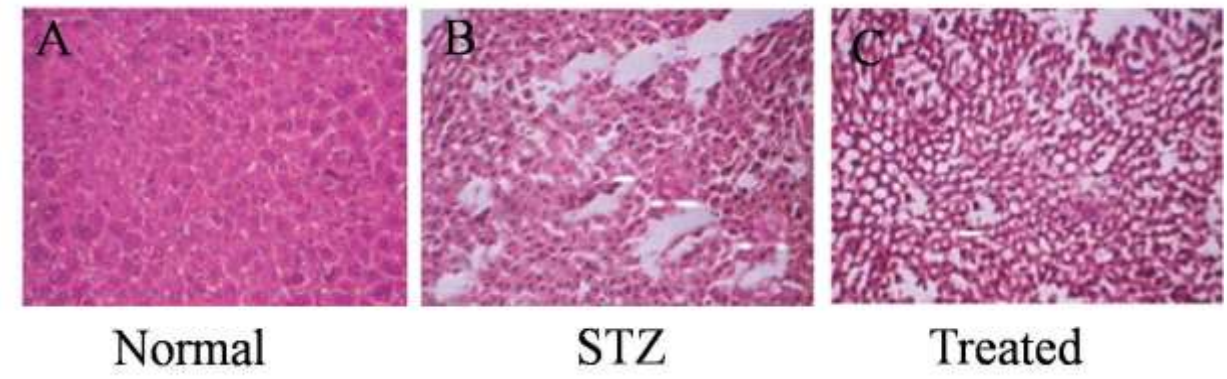

Table 2 represents the effect of ME on the serum TG, Cholesterol, HDL and LDL levels. After the treatment of ME triglyceride level were reduced and also a sharp reduction in serum triglycerides concentration after the treatment of reference drug. Furthermore ME also reduced the cholesterol and LDL but ME upregulate the level of HDL. This data exhibits the potent effect of ME on diabetes models.

Table 2: Effect of ***Murraya exotica*** (ME), **Metformin** (Met) and **Fenofibrate (**Ffb) on glucose, Triglyceride (TG), High density lipid (HDL) and Low density lipid (LDL) contents in streptozotocin (STZ) induced diabetes model (n= 6 in each group).*Statistically significant at P<0.05 and **P< 0.01, in comparison to control. n = 6 in each group.

Treatment	**TG mg/dl**	**Cholesterol mg/dl**	**HDL mg/dl**	**LDL mg/dl**
Control 1% CMC	398.5±66.48	278.6±33.34	58.00±08.48	75.00±13.76
ME (200 mg/kg)	314.5±30.89*	259.8±66.48	97.50±21.35*	58.20±8.22*
Metformin (100 mg/kg)	345.7±19.28	266.1±37.11	78.30±13.20*	72.50±9.918*
Fenofibrate (100 mg/kg)	261.2±22.01*	251.1±29.89	100.1±11.09*	52.50±11.84 **

Anti-oxidant effect of Murraya exotica:

The exquisite and consistent potency of compound ME in different experimental ulcer models prompted to choose it for further investigation. It was reported that oxygen free radicals were involved in the development of the ulceration in gastric mucosa. (Itoh and Guth, 1985) Antioxidants can reduce the oxidative stress and consequently, diminish the progress of stress related diseases like gastric ulceration (Hiraishi et al., 1999). Thus, the antioxidant study of compound ME was carried to find out its effect on free radicals and reactive oxygen species. Results revealed that compound ME had the property to scavenge the free radicals and reactive oxygen species in a dose dependent manner in DPPH (1,1-diphenyl-2-picryl-hydrazyl) and Superoxide dismutase (SOD) assays as discussed below. The potent antioxidant activity exhibited by the ME has beneficial implications to play a role in the relief of the oxidative stress and long- term chronic complications that are associated with ulcer pathogenesis.

In vitro anti oxidant property of Murraya exotica:

The ME exhibited strong antioxidant activity in the DPPH inhibition assay as evidenced by the low IC_{50} values 71.22 ±1.*72* µg/ml (Table 3). Whereas, the positive control ascorbic acid showed 38.87±3.10 µg/mL in the DPPH inhibition assays.

Table 3: Values are expressed as percentage mean of 3 replicates

Concentration (µg/ml)	1,1-diphenyl 1-2-picryl-hydrazyl (DPPH)
10	10.73 ± 1.24
20	27.70 ± 3.59
40	35.91 ± 4.10
60	48.06 ± 8.16
80	53.87 ± 12.73
100	70.25 ± 10.08
IC_{50} of ME	71.22 ± 1.72
Reference (Ascorbic acid)IC_{50}	38.87 ± 3.10

In vivo anti-oxidant property of Murraya exotica:

Superoxide dismutase (SOD) was assayed according to Misra and Fridevich (1972) based on the inhibition of epinephrine auto-oxidation by the enzyme. In the control group the SOD activities were 0.079 ± 0.35(U/mg protein) after the treatment with ***Murraya exotica*** it increases the SOD activity 0.312 ± 0.84 (U/mg protein) similar to reference antioxidant ascorbic acid treated group's SOD 0.346 ± 0.21 (P <0.01, when compared with control).

3.2 Discussion

Natural products brought substantial contributions to drug innovation by providing novel chemical structures and/or mechanisms of action (Rates, 2001). In India; a large number of herbal extracts are used in folk medicine to treat various types of disorders. The present study has been conducted to evaluate the anti-diabetic activity of *Murrya exotica* extract against STZ models of experimentally induced diabetes and to evaluate its mechanism of action involved in impediment of hyper/hypoglycemic development.

A preliminary study for the dose fixation of *Murrya exotica crude* extract was conducted and 200mg/kg was found to be the optimum dose that can give the highest protection. The screening results were summarized in the table 1. Sreptozotocin induced diabetic model is a well-accepted model for the induction of diabetes. Streptozotocin-induced diabetic murine models develop type 1 diabetes, due to the cytotoxic glucose analogue streptozotocin (STZ) that is toxic to pancreatic β-cells and causes insulin deficiency. STZ methylates DNA, causing DNA fragmentation and killing pancreatic β-cells. STZ related animal experiments appear to be a very good mimic of the human condition and have allowed studies into pathogenic mechanisms as well as useful therapeutic intervention. Thus, the significant protection imparted by ME in this model reflected the possibility of its involvement in the regulatory mechanism of diabetes. This interesting finding in STZ model intrigued to further explore its effects on other blood parameters of diabetic models in rats.

The effects of the ME on STZ induced and glucose level was examined and compared with the reference drug metformin (Table 2). Insulin and glucose plays a central role in diabetes. It is well known that reduction in insulin causes hyperglycemia. STZ has widely been used to induce diabetes in animals. It is a β-cell-specific toxin that induces irreversible damage to pancreatic islets through free radical generation and DNA damage. Besides, nitroso-containing STZ also releases nitric oxide that causes apoptosis.

Antioxidants can reduce the oxidative stress and consequently ameliorate the progress of stress related diseases. An *in vitro* and *in vivo* antioxidant study of ME was carried out to find out its antioxidant properties. Results revealed that ME had property to scavenge the free radicals and reactive oxygen species in a dose dependent manner in DPPH and SOD assays. The antioxidant activity of the ME was suggested to play a role in the relief of long-term complications and the oxidative stress.

CONCLUSION

This study explains evidence based-information regarding the antidiabetic activity of ethanol extract of ME in STZ models. It was obvious from the result that, the ethanol extract of ME played a beneficial role. In conclusion, leaves of ME inhibit the formation of diabetes in rats by inhibiting glucose level through the inhibition of insulin hormone. ME also exhibit anti-oxidative properties by scavenging the free radicals and reactive oxygen species. ME might be a potent therapeutic agent in treating diabetes incidences since it possesses anti- diabetic activity. **Murraya exotica** results shown in this study indicated that the **Murraya exotica** extract are most active against STZ induced diabetes model. Further potent anti-oxidant activity of Murraya exotica exhibiting there strong anti-diabetic effect in streptozotocin induced diabetic rats and could therefore be used as a remedy for the treatment of diabetes mellitus.

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